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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,266	06/20/2003	Fumitoshi Asai	17620-105003	7488

65989 7590 07/27/2011

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EXAMINER	
DRAPER, LESLIE ALEXANDRA R	
ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
07/27/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)
	10/600,266	ASAI ET AL.
	Examiner	Art Unit
	Leslie A. Royds Draper	1629

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *16May11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5 are presented for examination.

Applicant's Amendment and Information Disclosure Statement (IDS) filed May 16, 2011 have each been received and entered into the present application. As reflected by the attached, completed copy of form PTO/SB/08a (eight pages total), the Examiner has considered the cited references, except for the Holmes et al. reference at p.4 of IDS filed May 16, 2011 because Applicant failed to furnish a copy of said reference. The information disclosure statement filed May 16, 2011 fails to fully comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The IDS has been considered insofar as copies of the other cited references have been provided. However, the information referred to therein as the "Holmes et al." reference has not been considered.

Claims 1-5 remain pending and under examination. Claims 1-2 and 4-5 are amended.

Applicant's arguments, filed May 16, 2011, have been fully considered. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The newly added limitation "formulated with two active ingredients" as now presented in instant claim 1 renders the claim(s) indefinite because it is unclear if Applicant intends for the claimed pharmaceutical composition to be defined using product-by-process construction (as a result of the newly added limitation "formulated with"; see MPEP §2113) or if it is intended to be a definition of what is contained therein the claimed pharmaceutical composition rather than how it is formulated. This ambiguity in the claim(s) fails to clearly set forth what, in fact, comprises the claimed pharmaceutical composition and, thus, fails to clearly, precisely or deliberately define the metes and bounds of the subject matter for which Applicant is presently seeking protection. Clarification is required.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Applicant defines the claimed pharmaceutical composition as consisting of two compounds, i.e., the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine or a pharmaceutically acceptable salt thereof, and aspirin, in pharmacologically effective amounts. Thus, the composition as defined in claim 1 is closed to the incorporation of additional elements as a result of the use of the transitional phrase "consisting of". However, in instant claim 2, Applicant defines the composition as further comprising one or more pharmaceutically acceptable excipients, lubricants, binders, disintegrators, emulsifiers, stabilizers, corrigents and/or diluents, which conflicts with the closed language employed in instant claim 1. A composition that is defined to exclude additional elements (such as, e.g., instant claim 1) cannot then later add an additional element(s), such as those elements now recited in instant claim 2. This conflicting limitation now presented in instant claim 2 complicates the interpretation of the instant claims because it is unclear if Applicant intends for the

composition to be closed or open to additional elements. See MPEP §2111.03[R-3]. Clarification is required.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernat et al. (U.S. Patent No. 5,989,578; 1999) in view of Asai et al. ("CS-747, a New Platelet ADP Receptor Antagonist", *Annu. Rep. Sankyo Res. Lab.*, 1999; 51:1-44, cited by Applicant) and Koike et al. (U.S. Patent No. 5,288,726; 1994, already of record).

Bernat et al. teaches a pharmaceutical composition comprising clopidogrel with aspirin, each being present in the free form or in the form of a pharmaceutically acceptable salt (abstract), wherein the composition has anti-platelet aggregation activity (col.1, l.5-8). Bernat et al. teaches that the dose for each

of the components ranges from 1 to 500 mg/day, depending on the age of the subject to be treated and the purpose of the treatment (i.e., a "pharmacologically effective amount" as instantly claimed; col.3, l.18-20). Bernat et al. discloses that the compositions may be administered in unit forms for administration mixed with conventional pharmaceutical carriers (col.3, l.34-39), e.g., vehicles such as gelatin, starch, etc. for tablets; diluents for gelatin capsules; etc. (col.3, l.47-col.4, l.13).

Bernat et al. fails to teach (1) the use of the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in a pharmacologically effective amount (claim 1) or (2) the use of the hydrochloride or maleate salt(s) of the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (claims 4-5).

Asai et al. teaches that the compound CS-747 (also known as 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine) was identified as an antithrombotic that is an active antiplatelet drug with ADP-specific action, but with fewer side effects compared to clopidogrel or ticlopidine (p.3, col.2, para.2). Asai et al. teaches that CS-747 was determined to be an orally effective platelet aggregation inhibitor with high potency, fast onset and long duration of action (p.3, col.2, para.2) and comparative toxicologic studies determined that CS-747 was less toxic than clopidogrel and has a wide safety margin (p.4, col.2, para.2).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to employ the compound CS-747 (also known as 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine) compound, which is disclosed in the prior art as an effective platelet aggregation inhibitor with high potency, fast onset and long duration of action and less toxicity as compared to clopidogrel as evidenced by Asai et al., in place of the clopidogrel compound of the pharmaceutical composition of Bernat et al. to elicit the predictable result of producing a pharmaceutical composition with platelet aggregation inhibitory activity, but with the advantage of having a more rapid onset of action, longer duration of action and reduced toxicity. Such a person would

have been clearly motivated to do so in order to predictable generate an antiplatelet aggregation composition while reducing the incidence of concomitant toxicity as a result of the active agent(s), as well as to reduce the frequency of administration as a result of a longer duration of action. As stated in the MPEP at §2144.06, "An express suggestion to substitute one equivalent compound or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

Koike et al. teaches tetrahydrothienopyridine compounds and salts thereof (abstract), including the specifically named compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (col.22, l.19-21), wherein Koike et al. discloses that the compounds may be formulated in pharmaceutically acceptable acid addition salts, including, *inter alia*, the hydrochloric acid addition salt (i.e., hydrochloride salt) or the maleic acid addition salt (i.e., maleate salt) (col.13, l.43-63).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to employ the hydrochloride and/or maleate salt of the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the composition of Bernat et al. in view of Asai et al. because Koike et al. teaches that the hydrochloride or maleate salt is one of a finite number of pharmaceutically acceptable salts of the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine that were known in the art at the time of the invention to predictably function as tetrahydrothienopyridine inhibitors of blood platelet aggregation. Thus, one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to employ any of the known pharmaceutically acceptable salts of the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (which, as evidenced by Koike et al., included the hydrochloride and/or maleate salts) into this formulation of Bernat et al. in view of Asai et al. with a reasonable expectation of success because (1) a person with ordinary skill in the

art has good reason to pursue known options within his or her technical grasp and (2) Koike et al. teaches the functional equivalency of the compound 2-acetoxy-5-(α-cyclopropylcarbonyl-2-fluorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine and pharmaceutically acceptable salt(s) thereof to accomplish the inhibition of blood platelet aggregation.

Conclusion

Rejection of claims 1-5 is proper.

No claims of the present application are allowed.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP §714.02 and §2163.06). Note that support should be provided for amendments to previously pending claims, as well as any newly added claims. In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, not the published application. Due to the procedure outlined in MPEP §2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. §102 or 35 U.S.C. §103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims and share an inventor or assignee with the instant application. A copy of such copending claims is requested in response to this Office action in order to assist the examiner with double patenting analysis in the application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the

mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds Draper whose telephone number is (571)272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey S. Lundgren can be reached on (571)-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds Draper/
Primary Examiner, Art Unit 1629

July 19, 2011